Remarks/Arguments

Reconsideration of the above-identified application in view of the present amendment is respectfully requested.

By the present amendment, claims 1, 17, and 29 have been amended, claims 2, 3, 18, 30-31, 34, 36, and 55 have been cancelled, and claim 56 has been added.

Amended claim 1 recites a method of reducing glycosaminoglycan (GAG) content in a glial scar of a mammal comprising administering to the glial scar of the mammal an agent that inhibits the expression and/or activity of a chain initiation enzyme; wherein the agent is selected from the group consisting of antisense oligonucleotides, ribozymes, DNA enzymes, and RNAi constructs, the agent targeting a nucleic acid sequence encoding xylotransferase I (XT-I) or xylotransferase II (XT-II); wherein the agent is administered intrathecally, topically, or locally to the glial scar. Support for amended claim 1 can be found at p. 5, ll. 15-19, p. 5, ll. 26-30 to p. 6, ll. 1-2, p. 6, ll. 10-15, p. 49, ll. 15-24, p. 85, ll. 21-23, and p. 87, ll. 29-31 of the present application.

Amended claim 17 recites a method for promoting neuronal regeneration in a subject comprising administering an agent to a nervous system lesion to inhibit a GAG chain initiation enzyme, wherein the agent is selected from the group consisting of antisense oligonucleotides, ribozymes, DNA enzymes, and RNAi constructs, the agent targeting a nucleic acid sequence encoding XT-I or XT-II; wherein the agent is administered intrathecally, topically, or locally to the nervous system lesion; wherein the neuronal regeneration includes neurite extension into the

nervous system lesion. Support for amended claim 17 can be found at p. 5, ll. 15-19, p. 5, ll. 26-30 to p. 6, ll. 1-2, p. 6, ll. 10-15, p. 49, ll. 15-24, p. 85, ll. 21-23, and p. 87, ll. 29-31 of the present application.

Amended claim 29 recites a method for identifying and/or characterizing an agent, the method comprising screening a library of agents capable of one or more of the following: (i) inhibiting the expression of a primary proteoglycan; (ii) inhibiting the expression and/or activity of a chain initiation enzyme; (iii) inhibiting the expression and/or activity of a chain elongation enzyme; or (iv) promoting inter-mixing of Schwann cells and astrocytes. Support for amended claim 29 can be found at p. 3, ll. 12-19, and p. 21, ll. 5-7 of the present application.

New claim 56 depends directly from claim 29 and includes the further feature that the primary proteoglycan is selected from the group consisting of neurocan, NG2, and phosphacan. Support for new claim 56 can be found at p. 4, ll. 1-2 of the present application.

Below is a discussion of the objection to claim 18, the 35 U.S.C. §112, second paragraph, rejection of claim 30, the 35 U.S.C. §112, first paragraph, rejection of claims 1-3, 12-13, 17-18, 23-31, 34 and 36, the 35 U.S.C. §112, first paragraph, rejection of claims 1-3, 12-13, 17-18, 23-28, 36 and 55, the 35 U.S.C. §103(a) rejection of claims 29, 34 and 36, and the 35 U.S.C. §103(a) rejection of claims 29-31, 34 and 36.

1. Objection to claim 18.

The Office Action objected to claim 18 because the claim includes a grammatical error. The Office Action argues that the term "comprising" should properly be "comprises."

Claim 18 has been cancelled by the present amendment. Accordingly, Applicants respectively submit that the objection to claim 18 is rendered moot.

2. 35 U.S.C. §112, second paragraph, rejection of claim 30.

Claim 30 was rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. The Office Action argues that it is unclear how claim 30 further limits claim 29. In particular, the Office Action argues that it is unclear whether the phrase "promoting neurite extension" is a property/characteristic of the agent or a further requirement of the method.

Claim 30 has been cancelled by the present amendment. Accordingly, Applicants respectively submit that the 35 U.S.C. §112, second paragraph, rejection of claim 30 is rendered moot.

3. 35 U.S.C. §112, first paragraph, rejection of claims 1-3, 12-13, 17-18, 23-31, 34 and 36.

Claims 1-3, 12-13, 17-18, 23-31, 34, and 36 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The Office Action has maintained the rejection of claims 1-3, 12-13, 17-18, 23-31, 34, and 36 made in the previous Office Action (dated March 26, 2007), but has narrowed the rejection to cover only the delivery method. The Office Action acknowledges that

intrathecal and topical administration of various therapeutic nucleic acids is fully enabled. The Office Action argues, however, that the rejected claims are not enabled for methods of administration other than topical or intrathecal administration.

By the present amendment, claims 1 and 17 have amended to recite the further feature that the agent is administered intrathecally, topically, or locally. Support for amended claims 1 and 17 can be found at p. 87, line 29 to p. 88, line 4 of the present application. Accordingly, Applicants respectively submit that claims 1 and 17 are fully enabled for intrathecal, topical, and local delivery routes, and request that the 35 U.S.C. §112, first paragraph, rejection of claims 1 and 17 be withdrawn. Applicants also respectively request that the U.S.C. §112, first paragraph, rejection of claims 2 and 28, which depend either directly or indirectly from claims 1 and 17, be withdrawn.

Applicants respectfully point out that claim 29 does not recite the feature that an agent is administered to a glial scar. Rather, claim 29 recites a method of identifying and/or characterizing an agent. Accordingly, Applicants respectively submit that claim 29 is fully enabled as it presently stands.

Applicants respectively submit that the 35 U.S.C. §112, first paragraph, rejection of claims 30-31, 34, and 36 is rendered moot by the present amendment.

4. 35 U.S.C. §112, first paragraph, rejection of claims 1-3, 12-13, 17-18, 23-28, 36 and 55.

Claims 1-3, 12-13, 17-18, 23-28, 36, and 55 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Office Action argues that while the specification supports the broad definition of

agents as encompassing antisense oligonucleotides, ribozymes, DNA enzymes, RNAi constructs, and small molecules, the only demonstration of the claimed *in vivo* methods utilized DNA enzymes directed to XT-I and XT-II. The Office Action also argues that the specification does not support the genus recited in claims 1 and 17 because of the breadth of the agents encompassing the ribozymes, DNA enzymes, RNAi constructs, and small molecules.

The Office Action points out that antisense molecules, ribozymes, and DNA enzymes that bind a nucleic acid sequence encoding either XT-I or XT-II are sufficiently described in the specification. Additionally, the Office Action recommends that claims 1 and 17 be amended so that ribozymes, DNA enzymes, and RNAi constructs are also included with the antisense oligonucleotides as targeting specific nucleotide sequences encoding XT-I or XT-II. By the present amendment, claims 1 and 17 have been amended to recite that the agent is selected from the group consisting of antisense oligonucleotides, ribozymes, DNA enzymes, and RNAi constructs, the agent targeting a nucleic acid sequence encoding XT-I or XT-II.

Accordingly, Applicants respectively request that the 35 U.S.C. §112, first paragraph, rejection of claims 1 and 17 be withdrawn. Applicants also respectively request that the 35 U.S.C. §112, first paragraph, rejection of claims 2, 12-13, and 23-28, which depend either directly or indirectly from claims 1 and 17, be withdrawn.

Applicants respectively submit that the 35 U.S.C. §112, first paragraph, rejection of claims 18, 36, and 55 is rendered moot by the present amendment.

5. 35 U.S.C. §103(a) rejection of claims 29, 34 and 36.

Claims 29, 34, and 36 were rejected under 35 U.S.C. §103(a) as being obvious over U.S. Patent Pub. No. 2001/0049360 A1 to Vale *et al.* (hereinafter, "Vale"). The Office Action argues that Vale teaches a method for screening a library of probes capable of inhibiting expression of betaglycan by antisense inhibition. The Office Action acknowledges that Vale does not teach a pharmaceutical preparation of the agent. The Office Action then argues that it would have been obvious to make a pharmaceutical preparation because preparation of an agent into a pharmaceutical composition is common, if not required, for use as therapy.

Claim 29 is not obvious over Vale because Vale does not teach or suggest a method for screening a library of agents capable of inhibiting the expression of a primary proteoglycan. Vale teaches a method for screening compounds which inhibit formation of inhibin/betaglycan complexes (¶0071). Mature betaglycan is a proteoglycan which contains both heparan sulfate and chondroitin sulfate GAG chains (¶0016). Vale also discloses that inhibition of inhibin/betaglycan complexes can augment activin signaling (¶0021). Vale does not teach or suggest, however, a method for screening compounds capable of inhibiting betaglycan expression. Rather, the method of Vale is directed to a screen for compounds that inhibit the formation of a protein complex, *i.e.*, inhibin/betaglycan complexes.

Accordingly, Applicants respectively submit that Vale does not teach or suggest a method for screening a library of agents capable of inhibiting the expression of a primary proteoglycan, and request that the 35 U.S.C. §103(a) rejection of claim 29 be withdrawn.

Applicants also respectively submit that the 35 U.S.C. §103(a) rejection of claims 34 and 36 is rendered moot by the present amendment.

6. **35 U.S.C. §103(a) rejection of claims 29-31, 34 and 36.**

Claims 29-31, 34, and 36 were rejected under 35 U.S.C. §103(a) as being obvious over PCT Pub. No. WO/0073509 to Hodgson et al. (hereinafter, "Hodgson") in view of Taylor *et al.*, *Drug Discovery Today* 4(12):562-567, 1999 (hereinafter, "Taylor"). The Office Action argues that Hodgson teaches a method of screening compound libraries for diagnostic and therapeutic molecules, such as heparin-sulfate-6-sulfotransferase. The Office Action also argues that Taylor teaches a high-throughput method for screening antisense oligonucleotides. From this, the Office Action concludes that it would have been obvious to use a combination of these elements in a method of identifying agents capable of inhibiting expression of chain sulfation enzymes.

By the present amendment, claim 29 has been amended to recite a method for identifying and/or characterizing an agent comprising screening a library of agents capable of one or more of the following: (i) inhibiting the expression of a primary proteoglycan; (ii) inhibiting the expression and/or activity of a chain initiation enzyme; (iii) inhibiting the expression and/or activity of a chain elongation enzyme; or (iv) promoting inter-mixing of Schwann cells and astrocytes.

Claim 29 is not obvious over Hodgson in view of Taylor because the combination of Hodgson and Taylor does not teach or suggest a method for screening a library of agents capable of: (i) inhibiting the expression of a primary proteoglycan; (ii) inhibiting the expression and/or activity of a chain initiation enzyme;

(iii) inhibiting the expression and/or activity of a chain elongation enzyme; or (iv) promoting inter-mixing of Schwann cells and astrocytes. Hodgson discloses a method for screening a library of compounds capable of affecting the activity and/or expression of various molecules, including chain sulfation enzymes such as heparin-sulfate-6-sulfotransferase. By the present amendment, Applicants have removed the feature from claim 29 that the agent is capable of inhibiting the expression and/or activity of a chain sulfation enzyme. Neither Hodgson nor Taylor teach or suggest a method for screening a library of agents capable of: (i) inhibiting the expression of a primary proteoglycan; (ii) inhibiting the expression and/or activity of a chain initiation enzyme; (iii) inhibiting the expression and/or activity of a chain elongation enzyme; or (iv) promoting inter-mixing of Schwann cells and astrocytes.

Accordingly, Applicants respectively submit that claim 29 is not obvious over Hodgson in view of Taylor, and request that the 35 U.S.C. §103(a) rejection of claim 29 be withdrawn.

Applicants also respectively submit that the 35 U.S.C. §103(a) rejection of claims 30, 34, and 36 is rendered moot by the present amendment.

Please charge any deficiency or credit any overpayment in the fees for this matter to our Deposit Account No. 20-0090.

Respectfully submitted,

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